

What Is Claimed Is:

1. Cruciferous sprouts, with the exception of cabbage, cress, mustard and radish sprouts, harvested prior to the 2-leaf stage.
2. The cruciferous sprouts according to claim 1, wherein said sprouts are a *Brassica oleracea* selected from the group of varieties consisting of *acephala*, *alboglabra*, *botrytis*, *costata*, *gemmifera*, *gongylodes*, *italica*, *medullosa*, *palmifolia*, *ramosa*, *sabauda*, *sabellica*, and *selensia*.
3. The cruciferous sprouts according to claim 2, wherein said sprouts are a *Brassica oleracea* variety *italica*.
4. The cruciferous sprouts according to claim 1, wherein said sprouts are a *Brassica oleracea* variety *botrytis*.
5. The cruciferous sprouts according to claim 1, wherein said sprouts are a *Brassica oleracea* variety *botrytis* subvariety *cauliflora*.
6. The cruciferous sprouts according to claim 1, wherein said sprouts are substantially free of Phase 1 enzyme-inducing potential.
7. A non-toxic solvent extract of the cruciferous sprouts according to claim 1.
8. The non-toxic solvent extract according to claim 7, wherein said solvent is water.
9. The non-toxic solvent extract according to claim 8, further comprising a cruciferous vegetable comprising an active myrosinase enzyme.

10. The non-toxic solvent extract according to claim 9, wherein said cruciferous vegetable is of the genus *Raphanus*.

11. A method of increasing the chemoprotective amount of Phase 2 enzymes in a mammal, comprising the step of administering an effective quantity of the cruciferous sprouts according to claim 1.

12. Cruciferous sprouts harvested prior to the 2-leaf stage, wherein said sprouts have at least 200,000 units per gram fresh weight of Phase 2 enzyme-inducing potential when measured after 3-days of growth from seeds that produce said sprouts and non-toxic levels of indole glucosinolates and their breakdown products and goitrogenic hydroxybutenyl glucosinolates.

13. The cruciferous sprouts according to claim 12, wherein said sprouts are a *Brassica oleracea* selected from the group of varieties consisting of *acephala*, *alboglabra*, *botrytis*, *costata*, *gemmafera*, *gongylodes*, *italica*, *medullosa*, *palmifolia*, *ramosa*, *sabauda*, *sabellica*, and *selessia*.

14. The cruciferous sprouts according to claim 13, wherein said sprouts are a *Brassica oleracea* variety *italica*.

15. The cruciferous sprouts according to claim 13, wherein said sprouts are a *Brassica oleracea* variety *botrytis*.

16. The cruciferous sprouts according to claim 15, wherein said sprouts are a *Brassica oleracea* variety *botrytis* subvariety *cauliflora*.

17. A non-toxic solvent extract of the cruciferous sprouts according to claim 12.

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18. The non-toxic solvent extract according to claim 17, wherein said solvent is water.

19. The non-toxic solvent extract according to claim 18, further comprising a cruciferous vegetable comprising an active myrosinase enzyme.

20. The non-toxic solvent extract according to claim 19, wherein said cruciferous vegetable is of the genus *Raphanus*.

21. A method of preparing a food product rich in glucosinolates, comprising germinating cruciferous seeds, with the exception of cabbage, cress, mustard and radish seeds, and harvesting sprouts prior to the 2-leaf stage, to form a food product comprising a plurality of sprouts.

22. The method according to claim 21, wherein said sprouts contain non-toxic levels of indole glucosinolates and their breakdown products and goitrogenic hydroxybutenyl glucosinolates.

23. The method according to claim 21, wherein said seeds are a *Brassica oleracea* selected from the group of varieties consisting of *acephala*, *alboglabra*, *botrytis*, *costata*, *gemnifera*, *gongylodes*, *italica*, *medullosa*, *palmifolia*, *ramosa*, *sabauda*, *sabellica*, and *selensia*.

24. The method according to claim 23, wherein said seeds are *Brassica oleracea* variety *italica*.

25. The method according to claim 23, wherein said seeds are *Brassica oleracea* variety *botrytis*.

26. The method according to claim 25, wherein said seeds are *Brassica oleracea* variety *botrytis* subvariety *cauliflora*.

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~~27.~~ A food product rich in glucosinolates made by the process according to claim 21.

~~28.~~ A method of preparing a food product, comprising extracting glucosinolates and isothiocyanates from ~~cruciferous sprouts, according to claim 1~~ ^{with the exception of cabbage, cress, mustard and radish sprouts, harvested prior to the 2-leaf stage,} with a non-toxic solvent, removing the extracted sprouts from said solvent, and recovering the extracted glucosinolates and isothiocyanates.

~~29.~~ A method of preparing a food product according to claim ~~28~~, wherein active myrosinase enzyme is mixed with said cruciferous sprouts, or said extracted glucosinolates and isothiocyanates, or both said cruciferous sprouts or said extract.

~~30.~~ A method of preparing a food product rich in glucosinolates, comprising germinating cruciferous seeds that produce sprouts having at least 200,000 units per gram fresh weight of Phase 2 enzyme-inducing potential when measured after 3-days of growth and which contain non-toxic levels of indole glucosinolates and their breakdown products and goitrogenic hydroxybutenyl glucosinolates, and harvesting sprouts prior to the 2-leaf stage to form a food product comprising a plurality of sprouts.

~~31.~~ The method according to claim ~~30~~, wherein said seeds are a *Brassica oleracea* selected from the group of varieties consisting of *acephala*, *alboglabra*, *botrytis*, *costata*, *gemmifera*, *gongylodes*, *italica*, *medullosa*, *palmifolia*, *ramosa*, *sabauda*, *sabellica*, and *selensia*.

~~32.~~ The method according to claim ~~31~~, wherein said seeds are *Brassica oleracea* variety *italica*.

~~33.~~ The method according to claim ~~31~~, wherein said seeds are *Brassica oleracea* variety *botrytis*.

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~~34.~~ The method according to claim ¹²~~33~~, wherein said seeds are *Brassica oleracea* variety *botrytis* subvariety *cauliflora*.

~~35.~~ A food product rich in glucosinolates, made by the process according to claim 30.

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~~36.~~ A method of preparing a food product, comprising introducing cruciferous seeds, wherein said seeds produce sprouts having at least 200,000 units per gram fresh weight of Phase 2 enzyme-inducing potential when measured after 3-days of growth and non-toxic levels of indole glucosinolates and their breakdown products and goitrogenic hydroxybutenyl glucosinolates, into another edible ingredient.

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~~37.~~ A method of preparing a food product, comprising extracting glucosinolates and isothiocyanates with a non-toxic solvent and isothiocyanates from cruciferous seeds, sprouts, plants or plant parts wherein seeds that produce said sprouts, plant, or plant parts, have at least 200,000 units per gram fresh weight of Phase 2 enzyme-inducing potential when measured after 3-days of growth and wherein said seeds, sprouts, plants or plant parts have non-toxic levels of indole glucosinolates and their breakdown products and goitrogenic hydroxybutenyl glucosinolates, and recovering the extracted glucosinolates and isothiocyanates.

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~~38.~~ A method of preparing a food product according to claim ¹⁵~~37~~, wherein active myrosinase enzyme is mixed with said cruciferous seeds, sprouts or plants; or said extracted glucosinolates and isothiocyanates; or both said cruciferous seeds, sprouts or plants and said extract.

~~39.~~ A method of reducing the level of carcinogens in a mammal comprising administering to a mammal an

effective amount of cruciferous sprouts, with the exception of cabbage, cress, mustard and radish sprouts.

40. A method of reducing the level of carcinogens in a mammal, comprising administering to a mammal an effective amount of cruciferous sprouts having at least 200,000 units per gram fresh weight of Phase 2 enzyme-inducing potential when measured after 3-days of growth from seeds that produce said sprouts and non-toxic levels of indole glucosinolates and their breakdown products and goitrogenic hydroxybutenyl glucosinolates.

41. A method of extracting glucosinolates and isothiocyanates from plant tissue comprising the steps of homogenizing said plant tissue in an excess of a mixture of dimethyl sulfoxide, acetonitrile and dimethylformamide at a temperature sufficient to inactivate myrosinase enzyme activity.

42. A food product comprising cruciferous sprouts, with the exception of cabbage, cress, mustard and radish sprouts, harvested prior to the 2-leaf stage, cruciferous seeds; extracts of said sprouts or seeds; or any combination of said sprouts, seeds or extracts.

43. A method of increasing the chemoprotective amount of Phase 2 enzymes in a mammal, comprising the step of administering an effective quantity of the food product according to claim 42.

44. A food product comprising cruciferous sprouts harvested prior to the 2-leaf stage, wherein said sprouts have at least 200,000 units per gram fresh weight of Phase 2 enzyme-inducing potential when measured after 3-days of growth from seeds that produce said sprouts and non-toxic levels of indole glucosinolate and goitrogenic hydroxybutenyl glucosinolates; cruciferous seeds; extracts of said sprouts or seeds; or any combination of said sprouts, seeds or extracts.

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45. A method of increasing the chemoprotective amount of Phase 2 enzymes in a mammal, comprising the step of administering an effective quantity of the food product according to claim 44.

46. Cruciferous sprouts harvested prior to the 2-leaf stage, wherein the ratio of monofunctional to bifunctional inducers is at least 20 to 1.

47. A food product supplemented with a purified or partially purified glucosinolate.

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ABSTRACT OF THE DISCLOSURE

Sub B₁ →

Vegetable sources of cancer chemoprotective agents have been identified which are extraordinarily rich in glucosinolates, metabolic precursors of isothiocyanates. The vegetable sources are used to provide a dietary means of reducing the level of carcinogens in mammals.

Docket No. 46528/102/JOHO**DECLARATION AND POWER OF ATTORNEY**

As a below named inventor, I hereby declare that:

My residence, post office address, and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

CANCER CHEMOPROTECTIVE FOOD PRODUCTS

the specification of which (check one)

- ☒ is attached hereto
- ☐ was filed on _____ as Application Serial No. _____ and was amended on _____ (if applicable).

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is known by me to be material to patentability as defined in Title 37, Code of Federal Regulations § 1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, § 119 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed:

PRIOR FOREIGN APPLICATION(S)

NUMBER	COUNTRY	DAY/MONTH/YEAR FILED	PRIORITY CLAIMED

I hereby claim the benefit under Title 35, United States Code, § 120, of any United States application(s) listed below and insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, § 112, I acknowledge the duty to disclose information which is known by me to be material to patentability as defined in Title 37, Code of Federal Regulations § 1.56 which occurred between the filing date of the prior application and the national or PCT international filing date of this application:

APPLICATION SERIAL NO.	FILING DATE	STATUS: PATENTED, PENDING, ABANDONED

I hereby appoint as my attorneys, with full powers of substitution and revocation, to prosecute this application and transact all business in the Patent and Trademark Office connected therewith: Stephen A. Bent, Reg. No. 29,768; David A. Blumenthal, Reg. No. 26,257; John J. Feldhaus, Reg. No. 28,822; Donald D. Jeffery, Reg. No. 19,980; Eugene M. Lee, Reg. No. 32,039; Peter G. Mack, Reg. No. 26,004; Brian J. McNamara, Reg. No. 32,789; Sybil Mcloy, Reg. No. 22,749; George E. Quillin, Reg. No. 32,792; Colin G. Sandercock, Reg. No. 31,298; Bernhard D. Saxe, Reg. No. 28,665; Richard L. Schwaab, Reg. No. 25,479; Arthur Schwartz, Reg. No. 22,115; Harold C. Wegner, Reg. No. 25,258.

Send all correspondence to FOLEY & LARDNER, 3000 K Street, N.W., Suite 500, Washington, DC 20007-5109 / Address telephone communications to Bernhard D. Saxe at (202) 672-5300.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Full Name of First or Sole Inventor <u>Jed W. FAHEY</u>		Signature of First or Sole Inventor <u>Jed W. Fahey</u>	Date <u>5/13/95</u>
Residence Address <u>6704 RIDGE RD., ELDERSBURG, MD 21784</u>		Country of Citizenship <u>United States</u>	
Post Office Address <u>6704 RIDGE RD., ELDERSBURG, MD 21784</u>			

Signatures should conform to names as typewritten. ☒ Additional inventors on attached Page 2.

PAGE 2

Docket No. 46528/102/JOHO

20 Full Name of Second Inventor <u>Paul TALALAY</u>	Signature of Second Inventor <u>Paul Talalay</u>	Date <u>9/13/95</u>
Residence Address <u>5512 BOXHILL LANE, BALTIMORE MD 21210</u>	Country of Citizenship <u>United States</u>	
Post Office Address <u>5512 BOXHILL LANE BALTIMORE MD 21210</u>		

PRINT OF DRAWINGS
AS ORIGINALLY FILED

08/528858

Inducer Activity of Broccoli Sprouts Effect of Plant Age

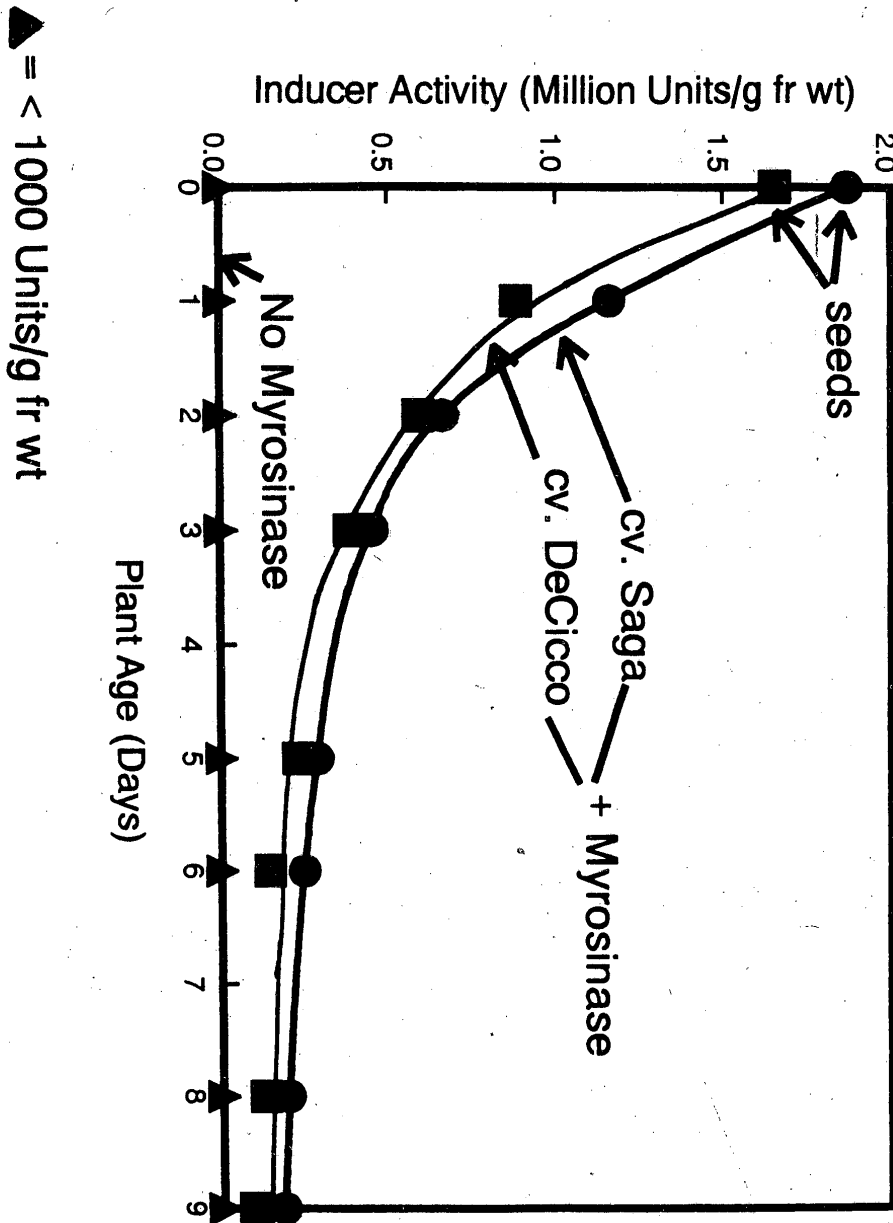
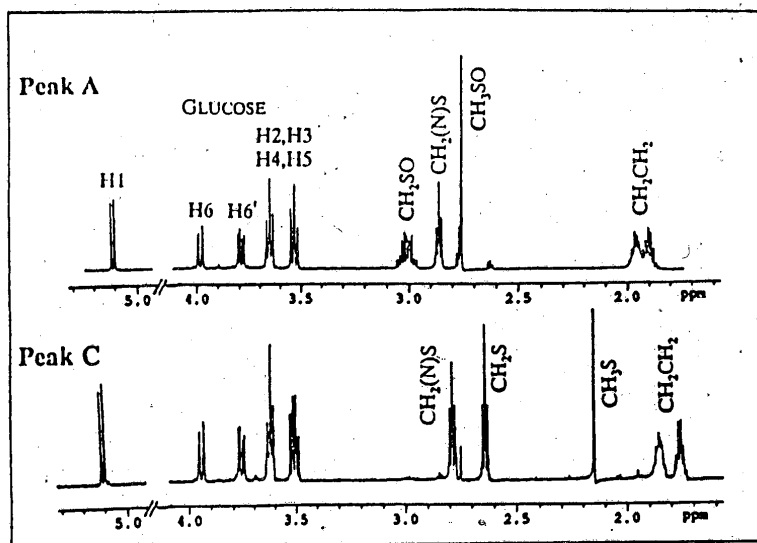


Figure 1

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PRINT OF DRAWINGS
AS ORIGINALLY FILED

08 528858



High Resolution NMR (600 MHz) in D₂O. Note: chirality of SO in Peak A induces multiplet for CH₂SO (Peak A), not observed for CH₂S (Peak C).

Figure 2

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1-31-96

85 Re- PCT/PTO 24 OCT 1995

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Wong
1-16



13x W29
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FC
REFUND
0260
0150

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

ATTN. FINANCE DEPARTMENT
REFUND DIVISION

In re Patent Application of
FAHEY et al.

Serial No.: 08/528,858

Group Art Unit: UNKNOWN

Filed: September 15, 1995

Examiner: UNKNOWN

For: CANCER CHEMOPROTECTIVE FOOD
PRODUCTS

REQUEST FOR REFUND

Commissioner of Patents and Trademarks
Washington, D. C. 20231

Sir:

A verified statement claiming small entity status
is filed concurrently herewith in connection with the
subject application.

The first fee in this application, paid on
September 15, 1995 in the amount of \$2,200.00 established
for a non-small entity. Therefore, Applicant is entitled
to a 50% refund of said fee, consistent with the Notice of
the Acting Commissioner of Patent and Trademarks of
February 15, 1983 (1027 OG 115).

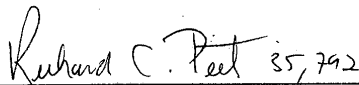
Therefore, the Patent and Trademark Office is
requested to make a refund in the form of a check in the
amount of \$1,100.00 forwarded to the undersigned at the

Serial No.: 08/528,858

address indicated below. This paper is being submitted in duplicate for the convenience of the Finance Branch.

Respectfully submitted,

October 24, 1995


Bernhard D. Saxe
Registration No. 28,665

FOLEY & LARDNER
3000 K Street, N.W.
Suite 500
Washington, D.C. 20007-5109
(202) 672-5300

#2

Applicant or Patentee: FAHEY et al.
 Serial or Patent No.: 08/528,858 Atty. Dkt. No. 46528/102/JOHO
 Filed or Issued: 9/15/95
 For: CANCER CHEMOPROTECTIVE FOOD PRODUCTS

**VERIFIED STATEMENT (DECLARATION) CLAIMING SMALL ENTITY STATUS
 (37 CFR 1.9(f) AND 1.27 (c)) — NONPROFIT ORGANIZATION**

I hereby declare that I am an official empowered to act on behalf of the nonprofit organization identified below:

NAME OF ORGANIZATION: Johns Hopkins School of Medicine
 ADDRESS OF ORGANIZATION: 2024 E. Monument Street, Suite 12-100, Baltimore, MD 21205
 TYPE OF ORGANIZATION:
☒ UNIVERSITY OR OTHER INSTITUTION OF HIGHER EDUCATION
☐ TAX EXEMPT UNDER INTERNAL REVENUE SERVICE CODE (26 USC 501(a) AND 501(c)(3))
☐ NONPROFIT SCIENTIFIC OR EDUCATIONAL UNDER STATUTE OF STATE OF THE UNITED STATES OF AMERICA
 (NAME OF STATE)
 (CITATION OF STATUTE)
☐ WOULD QUALIFY AS TAX EXEMPT UNDER INTERNAL REVENUE SERVICE CODE (26 USC 501(a) AND 501(c)(3)) IF LOCATED IN THE UNITED STATES OF AMERICA
☐ WOULD QUALIFY AS NONPROFIT SCIENTIFIC OR EDUCATIONAL UNDER STATUTE OF STATE OF THE UNITED STATES OF AMERICA IF LOCATED IN THE UNITED STATES OF AMERICA
 (NAME OF STATE)
 (CITATION OF STATUTE)

I hereby declare that the nonprofit organization identified above qualifies as a nonprofit organization as defined in 37 CFR 1.9(e) for purposes of paying reduced fees under section 41(a) or (b) of Title 35, United States Code with regard to the invention entitled CANCER CHEMOPROTECTIVE FOOD PRODUCTS by inventor(s) FAHEY et al. described in

☒ the specification filed herewith
☐ application serial no. _____, filed _____
☐ patent no. _____, issued _____

I hereby declare that rights under contract or law have been conveyed to and remain with the nonprofit organization with regard to the above-identified invention.

If the rights held by the nonprofit organization are not exclusive, each individual, concern or organization having rights to the invention is listed below* and no rights to the invention are held by any person, other than the inventor, who could not qualify as a small business concern under 37 CFR 1.9(d) or by any concern which would not qualify as a small business concern under 37 CFR 1.9(d) or a nonprofit organization under 37 CFR 1.9(e). *NOTE: Separate verified statements are required from each named person, concern or organization having rights to the invention averring to their status as small entities. (37 CFR 1.27)

NAME: _____
 ADDRESS: _____
☐ INDIVIDUAL ☐ SMALL BUSINESS CONCERN ☐ NONPROFIT CORPORATION

NAME: _____
 ADDRESS: _____
☐ INDIVIDUAL ☐ SMALL BUSINESS CONCERN ☐ NONPROFIT CORPORATION

I acknowledge the duty to file, in this application or patent, notification of any change in status resulting in loss of entitlement to small entity status prior to paying, or at the time of paying, the earliest of the issue fee or any maintenance fee due after the date on which status as a small entity is no longer appropriate: (37 CFR 1.28(b)).

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

NAME OF PERSON SIGNING: David A. Blake, Ph.D.
 TITLE OF PERSON OTHER THAN OWNER: Executive Vice Dean
 ADDRESS OF PERSON SIGNING: 3720 Rutland Avenue, Baltimore, Maryland 21205
 SIGNATURE: [Signature] DATE: 2-2-05

UNITED STATES PATENT & TRADEMARK OFFICE
Washington, D.C. 20231

REQUEST FOR PATENT FEE REFUND			
1 Date of Request: <u>11/14/95</u>		2 Serial/Patent # <u>08/528838</u>	
3 Please refund the following fee(s):		4 PAPER NUMBER	5 DATE FILED
<input checked="" type="checkbox"/>	Filing		9/15/95
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<input type="checkbox"/>	Issue		
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<input type="checkbox"/>	Assignment		
<input type="checkbox"/>	Other		
		7 TOTAL AMOUNT OF REFUND	\$ 76 -
10 REASON:		8 TO BE REFUNDED BY:	
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<input type="checkbox"/>	Duplicate Payment	<input type="checkbox"/>	Credit Deposit A/C #:
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11 REFUND REQUESTED BY:			
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OFFICE: <u>OICE</u>			
***** THIS SPACE RESERVED FOR FINANCE USE ONLY: *****			
APPROVED: <u>Paul Phillips</u>		DATE: <u>12-5-98</u>	

Instructions for completion of this form appear on the back. After completion, attach white and yellow copies to the official file and mail or hand-carry to:

13/21 1301
NOV 30 13
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

ATTY. DOCKET NO. 46528/102/JOHO



In re Patent Application of

FAHEY et al.

Serial No. 08/528,858

Group Art Unit:

Filed: September 15, 1995 Examiner:

For: CANCER CHEMOPROTECTIVE FOOD PRODUCTS

INFORMATION DISCLOSURE STATEMENT
UNDER 37 CFR 1.56

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Submitted herewith on Form PTO-1449 is a listing of documents known to Applicants in order to comply with Applicants' duty of disclosure pursuant to 37 CFR 1.56. A copy of each listed document is being submitted to comply with the provisions of 37 CFR 1.97 and 1.98.

The submission of any document herewith, which is not a statutory bar, is not intended as an admission that such document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in 37 CFR §1.56(b). Applicants do not waive any rights to take any action which would be appropriate to antedate or otherwise remove as a competent reference any document which is determined to be a prima facie prior art reference against the claims of the present application.

RECEIVED
OFFICE OF THE DIRECTOR
FEB 12 1996

DEC 14 1995

RECEIVED
OFFICE OF FINANCE
FEB 12 1996

Serial No. 08/528,858


CONCISE EXPLANATION OF
RELEVANCE OF EACH DOCUMENT

The relevance of the documents is described in the present specification.

The listed document is being submitted in compliance with 37 C.F.R. §1.97(b), within three (3) months of the filing date.

Applicants respectfully request that the listed documents be considered by the Examiner and formally be made of record in the present application and that an initialled copy of Form PTO-1449 be returned in accordance with MPEP §609.

Respectfully submitted,



Richard C. Peet
Reg. No. 35,792

December 14, 1995

FOLEY & LARDNER
3000 K Street, N.W.
Suite 500
Washington, D.C. 20007-5109
Tel: (202) 672-5300

[illegible]

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[illegible]

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered.
Include copy of this form with next communication to applicant.

[illegible]

[illegible]

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Include copy of this form with next communication to applicant.

[illegible]

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**UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office**

 Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NUMBER

FILING DATE

FIRST NAMED APPLICANT

ATTORNEY DOCKET NO.

08/528,858

09/15/95

FAHEY

J

46528/102/J0

EXAMINER

WONG, L.

13M1/0903

ART UNIT

PAPER NUMBER

 FOLEY AND LARDNER
3000 K STREET NW
SUITE 500
WASHINGTON DC 20007-5109
1302
DATE MAILED:

09/03/96

 This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS
OFFICE ACTION SUMMARY

- ☐ Responsive to communication(s) filed on _____
- ☐ This action is **FINAL**.
- ☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire _____ month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

- ☒ Claim(s) 1-47 is/are pending in the application.
- Of the above, claim(s) _____ is/are withdrawn from consideration.
- ☐ Claim(s) _____ is/are allowed.
- ☐ Claim(s) _____ is/are rejected.
- ☐ Claim(s) _____ is/are objected to.
- ☒ Claims 1-47 are subject to restriction or election requirement.

Application Papers

- ☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- ☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- ☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been
- ☐ received.
- ☐ received in Application No. (Series Code/Serial Number) _____
- ☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

- ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- ☐ Notice of Reference Cited, PTO-892
- ☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
- ☐ Interview Summary, PTO-413
- ☐ Notice of Draftsperson's Patent Drawing Review, PTO-948
- ☐ Notice of Informal Patent Application, PTO-152

1-C24

-- SEE OFFICE ACTION ON THE FOLLOWING PAGES --

Serial Number: 08/528858

Page 2

Art Unit: 1302

DETAILED ACTION

Election/Restriction

Restriction to one of the following inventions is required under 35 U.S.C. 121:

- I. Claims 1-6 and 12-16, drawn to cruciferous sprouts, classified in class 800, subclass 200.
- II. Claims 7-10 and 17-20, drawn to a solvent extract of cruciferous sprouts, classified in class 530, subclass 370.
- III. Claims 21-26, 28-34, and 36-38, drawn to a method of preparing a food product rich in glucosinolates, classified in class 426, subclass 049.
- IV. Claims 27, 35, 42, 44, and 47, drawn to a food product rich in glucosinolates, classified in class 426, subclass 615.
- V. Claims 39 and 40, drawn to a method of reducing the level of carcinogens in a mammal, classified in class 514, subclass 514.
- VI. Claim 41, drawn to a method of extracting glucosinolates and isothiocyanates from plant tissue, classified in class 530, subclass 370.
- VII. Claims 11, 43, and 45, drawn to a method of increasing the chemoprotective amount of Phase 2 enzymes in a mammal, classified in class 514, subclass 002+.
- VIII. Claim 46, drawn to cruciferous sprouts, classified in class 800, subclass 200.

The inventions are distinct, each from the other because of the following reasons:

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Art Unit: 1302

As between the subject matter of the claims of Group I and claims of Groups II, III, IV V, VI, VII, and VIII; as between the subject matter of the claims of Group II and the claims of Groups III, IV, V, VI, VII, and VIII; as between the subject matter of the claims of Group III and the claims of Groups IV, V, VI, VII, and VIII; as between the subject matter of the claims of Group V and the claims of Groups VI, VII, and VIII; as between the subject matter of the claims of Group VI and the claims of Groups VII and VIII; and as between the subject matter of the claims of Group VII and Group VIII, it is considered that each set of claims to the other are drawn to mutually exclusive subject matter. The requirements of one set of claims to the other are not mandatory.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification and their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

Applicant is advised that the response to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

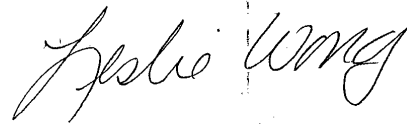
Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(h).

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Art Unit: 1302

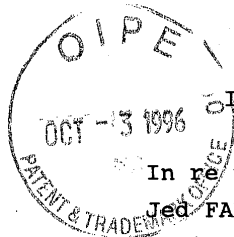
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leslie Wong whose telephone number is (703) 308-1979.

A handwritten signature in cursive script that reads "Leslie Wong".

LESLIE WONG
PRIMARY EXAMINER
GROUP 1300

LAW

August 29, 1996



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re patent application of
Jed FAHEY et al.

Serial No. 08/528,858

Group Art Unit: 1302

Filed: September 15, 1995

Examiner: L. Wong

For: CANCER CHEMOPROTECTIVE FOOD PRODUCTS

RESPONSE TO RESTRICTION REQUIREMENT

The Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

LW
8/9
Sir:

Responsive to the Office Action dated September 3, 1996, applicant hereby elects, with traverse, to prosecute claims 21-16, 28-34 and 36-38 of Group III in the above-identified application.

Applicants believe that it would not constitute an undue burden for the examiner to consider all claims in the pending application. In particular, the subject matter incorporated in the claims of Groups I, III and IV would require a search of similar scope. Accordingly, Applicants request that the examiner at least consider examining the claims of Groups I, III and IV together.

Applicants reserve the right to file one or more divisional applications for the non-elected subject matter.

Serial No. 08/528,858

Receipt of the initial office Action on the merits
is awaited.

Respectfully submitted,

October 3, 1996
Date

S. C. Peet Reg. No. 35,792
for Richard C. Peet
Reg. No. 35,792

FOLEY & LARDNER
3000 K Street, N.W.
Suite 500
Washington, D.C. 20006-5109
Tel: (202) 672-5300


**UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office**

 Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NUMBER: 13	09/1 FILING DATE FAHEY	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.: 107/10
------------------------	------------------------	-----------------------	-----------------------------

 13M1/1224
 FOLEY AND LARDNER
 3000 K STREET NW
 SUITE 500
 WASHINGTON DC 20007-5109

W/EXAMINER

ART UNIT 2 PAPER NUMBER

DATE MAILED:

12/31/96

 This is a communication from the examiner in charge of your application.
 COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY
☒ Responsive to communication(s) filed on 10/3/96
☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

 A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims
☒ Claim(s) 1-47 is/are pending in the application.

 Of the above, claim(s) 1-20, 27, 35, and 39-47 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 21-26, 28-34, 36, 37, and 38 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers
☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119
☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)
☒ Notice of Reference Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

1-C30

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Page 2

Art Unit: 1302

Applicant's election with traverse of Group III in Paper No. 5 is acknowledged. The traversal is on the ground(s) that examination of Group I, III, and IV would not constitute undue burden. This is not found persuasive because the inventions have recognized divergent subject matter.

The requirement is still deemed proper and is therefore made FINAL.

Claims 21-26, 28-34, and 36-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kenjirou (abstract of JP 60094056) in view of Beecher (Am. J. Clin. Nutr., A8), Zhang et al (A3), Zhang et al (A10), and Cho et al ('986).

Kenjirou disclose broccoli sprouts (see abstract). The production of sprouts (e.g. broccoli) is notoriously well-known.

The claims differ as to the specific recitation of glucosinolates/isothiocyanates.

Nothing patentable is seen here as Zhang et al disclose the anticarcinogenic activities of isothiocyanates (see pages 1976s-1981s).

Beecher discloses the cancer preventive properties of varieties of Brassica oleracea (see pages 1166s-1170s).

Zhang et al disclose a major inducer of anticarcinogenic protective enzymes from broccoli (see pages 2399-2403).

Cho et al disclose chemoprotective isothiocyanates (see entire patent).

It would have been obvious to a person of ordinary skill in the art, at the time the invention was made, that the process of preparing the product of Kenjirou would be rich in

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Page 3

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chemoprotective agents as Beecher, Zhang et al (A3), Zhang et al (A10), and Cho et al, all teach the cancer preventive properties of *Brassica*.

In the absence of unexpected results, it is not seen how the claimed invention differs from the teachings of the prior art. Applicant's claims are drawn to a combination of known components which produces expected results, see *In re Kerkhoven* 205 USPQ 1069 and *In re Gershon* 152 USPQ 602.

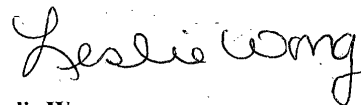
All of the claim limitations have been considered. None of them are seen as serving as basis for patentability.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leslie Wong whose telephone number is (703) 308-1979. The examiner can normally be reached on Tuesday-Thursday from 6:30 AM to 5:00 PM.

The fax number for this Group is (703) 305-3602.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0651.



Leslie Wong
Primary Examiner
Art Unit 1302

LAW
December 19, 1996

TO SEPARATE, HOLD TOP AND BOTTOM EDGES, SNAP-APART AND DISCARD CARBON

FORM PTO-892 (REV. 2-92)		U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE		SERIAL NO. 08/528858	GROUP/ART UNIT 1302	ATTACHMENT TO PAPER NUMBER 6	
NOTICE OF REFERENCES CITED				APPLICANT(S) Fahey et al.			
U.S. PATENT DOCUMENTS							
*	DOCUMENT NO.	DATE	NAME	CLASS	SUB-CLASS	FILING DATE IF APPROPRIATE	
A	5411986	5/95	Cho et al.	514	514		
B							
C							
D							
E							
F							
G							
H							
I							
J							
K							
FOREIGN PATENT DOCUMENTS							
*	DOCUMENT NO.	DATE	COUNTRY	NAME	CLASS	SUB-CLASS	PERTINENT SHTS. PP. DWG. SPEC.
L							
M							
N							
O							
P							
Q							
OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, Etc.)							
R							
S							
T							
U							
EXAMINER Leslie Wagon			DATE 12/19/96		1-C33		
<p style="text-align: center;">* A copy of this reference is not being furnished with this office action. (See Manual of Patent Examining Procedure, section 707.05 (a).)</p>							

Form PTO 948 (Rev. 10-94)

U.S. DEPARTMENT OF COMMERCE - Patent and Trademark Office

Application No.

528858

NOTICE OF DRAFTSPERSON'S PATENT DRAWING REVIEW

PTO Draftpersons review all originally filed drawings regardless of whether they are designated as formal or informal. Additionally, patent Examiners will review the drawings for compliance with the regulations. Direct telephone inquiries concerning this review to the Drawing Review Branch, 703-305-8404.

The drawings filed (insert date) 9/15/95, are
 A. not objected to by the Draftsperson under 37 CFR 1.84 or 1.152.
 B. not objected to by the Draftsperson under 37 CFR 1.84 or 1.152 as indicated below. The Examiner will require submission of new, corrected drawings when necessary. Corrected drawings must be submitted according to the instructions on the back of this Notice.

1. DRAWINGS. 37 CFR 1.84(a): Acceptable categories of drawings:

- Black ink. Color.
- Not black solid lines. Fig(s) _____
- Color drawings are not acceptable until petition is granted. Fig(s) _____

2. PHOTOGRAPHS. 37 CFR 1.84(b)

- Photographs are not acceptable until petition is granted. Fig(s) _____
- Photographs not properly mounted (must use bristol board or photographic double-weight paper). Fig(s) _____
- Poor quality (half-tone). Fig(s) _____

3. GRAPHIC FORMS. 37 CFR 1.84(d)

- Chemical or mathematical formula not labeled as separate figure. Fig(s) _____
- Group of waveforms not presented as a single figure, using common vertical axis with time extending along horizontal axis. Fig(s) _____
- Individual waveform not identified with a separate letter designation adjacent to the vertical axis. Fig(s) _____

4. TYPE OF PAPER. 37 CFR 1.84(c)

- Paper not flexible, strong, white, smooth, nonshiny, and durable. Sheet(s) _____
- Erasures, alterations, overwritings, interlineations, cracks, creases, and folds copy machine marks not accepted. Fig(s) 1, 2
- Mylar, velum paper is not acceptable (too thin). Fig(s) _____

5. SIZE OF PAPER. 37 CFR 1.84(f): Acceptable sizes:

- 21.6 cm. by 35.6 cm. (8 1/2 by 14 inches)
- 21.6 cm. by 33.1 cm. (8 1/2 by 13 inches)
- 21.6 cm. by 27.9 cm. (8 1/2 by 11 inches)
- 21.0 cm. by 29.7 cm. (DIN size A4)

- All drawing sheets not the same size. Sheet(s) _____
- Drawing sheet not an acceptable size. Sheet(s) _____

6. MARGINS. 37 CFR 1.84(g): Acceptable margins:

Paper size

21.6 cm. X 35.6 cm. (8 1/2 X 14 inches)	21.6 cm. X 33.1 cm. (8 1/2 X 13 inches)	21.6 cm. X 27.9 cm. (8 1/2 X 11 inches)	21.0 cm. X 29.7 cm. (DIN Size A4)
T 5.1 cm. (2")	2.5 cm. (1")	2.5 cm. (1")	2.5 cm.
L .64 cm. (1/4")	.64 cm. (1/4")	.64 cm. (1/4")	2.5 cm.
R .64 cm. (1/4")	.64 cm. (1/4")	.64 cm. (1/4")	1.5 cm.
B .64 cm. (1/4")	.64 cm. (1/4")	.64 cm. (1/4")	1.0 cm.

Margins do not conform to chart above.

Sheet(s)

Top (T) Left (L) Right (R) Bottom (B)

7. VIEWS. 37 CFR 1.84(h)

REMINDER: Specification may require revision to correspond to drawing changes.

- All views not grouped together. Fig(s) _____
- Views connected by projection lines or lead lines. Fig(s) _____
- Partial views. 37 CFR 1.84(h) 2

View and enlarged view not labeled separately or properly.

Fig(s) _____

Sectional views. 37 CFR 1.84 (h) 3

Hatching not indicated for sectional portions of an object.

Fig(s) _____

Cross section not drawn same as view with parts in cross section with regularly spaced parallel oblique strokes. Fig(s) _____

8. ARRANGEMENT OF VIEWS. 37 CFR 1.84(i)

- Words do not appear on a horizontal, left-to-right fashion when page is either upright or turned so that the top becomes the right side, except for graphs. Fig(s) _____

9. SCALE. 37 CFR 1.84(k)

- Scale not large enough to show mechanism with crowding when drawing is reduced in size to two-thirds in reproduction. Fig(s) _____
- Indication such as "actual size" or scale 1/2" not permitted. Fig(s) _____

10. CHARACTER OF LINES, NUMBERS, & LETTERS. 37 CFR 1.84(l)

- Lines, numbers & letters not uniformly thick and well defined, clean, durable, and black (except for color drawings). Fig(s) 2

11. SHADING. 37 CFR 1.84(m)

- Solid black shading areas not permitted. Fig(s) _____
- Shade lines, pale, rough and blurred. Fig(s) _____

12. NUMBERS, LETTERS, & REFERENCE CHARACTERS. 37 CFR 1.84(p)

- Numbers and reference characters not plain and legible. 37 CFR 1.84(p)(1) Fig(s) 2
- Numbers and reference characters not oriented in same direction as the view. 37 CFR 1.84(p)(1) Fig(s) _____
- English alphabet not used. 37 CFR 1.84(p)(2) Fig(s) _____

- Numbers, letters, and reference characters do not measure at least .32 cm. (1/8 inch) in height. 37 CFR(p)(3) Fig(s) 2

13. LEAD LINES. 37 CFR 1.84(q)

- Lead lines cross each other. Fig(s) _____
- Lead lines missing. Fig(s) _____

14. NUMBERING OF SHEETS OF DRAWINGS. 37 CFR 1.84(t)

- Sheets not numbered consecutively, and in Arabic numerals, beginning with number 1. Sheet(s) _____

15. NUMBER OF VIEWS. 37 CFR 1.84(u)

- Views not numbered consecutively, and in Arabic numerals, beginning with number 1. Fig(s) 2
- View numbers not preceded by the abbreviation Fig. Fig(s) _____

16. CORRECTIONS. 37 CFR 1.84(w)

- Corrections not made from prior PTO-948. Fig(s) _____

17. DESIGN DRAWING. 37 CFR 1.152

- Surface shading shown not appropriate. Fig(s) _____
- Solid black shading not used for color contrast. Fig(s) _____

COMMENTS:

- FIG. LEG. MUST BE PARALLEL TO

FIG.

(FIG. 1)

- REMOVE BOX AROUND FIG
(FIG. 2)

12/22/05



UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

08/528858

SERIAL NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKETT NO.
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9/15/95

Fahey et al.

46528/102/10

EXAMINER

L Wong

ART UNIT

PAPER NUMBER

1302

7

DATE MAILED:

EXAMINER INTERVIEW SUMMARY RECORD

All participants (applicant, applicant's representative, PTO personnel):

(1) Richard Peet (3) Jed. Fahey
(2) Paul Tabalay (4) Leslie Wong

Date of interview 3/11/97Type: ☐ Telephonic ☒ Personal (copy is given to ☐ applicant ☒ applicant's representative).Exhibit shown or demonstration conducted: ☒ Yes ☐ No. If yes, brief description: Presentation of the chemistry and benefits of the application.Agreement ☒ was reached with respect to some or all of the claims in question. ☐ was not reached.Claims discussed: allIdentification of prior art discussed: that cited, especially Japanese reference (Kenjiro)

Description of the general nature of what was agreed to if an agreement was reached, or any other comments: Discussed applicability of cited references, especially Kenjiro. It appears that Kenjiro is an improper translation. Applicant will provide support for proof of improper translation and will also provide

(A fuller description, if necessary, and a copy of the amendments, if available, which the examiner agreed would render the claims allowable must be attached. Also, where no copy of the amendments which would render the claims allowable is available, a summary thereof must be attached.)

☒ 1. If it is not necessary for applicant to provide a separate record of the substance of the interview, rejection for presentation material. It appears that pending further search the claims will be allowed over the prior art of record.

Unless the paragraph below has been checked to indicate to the contrary, A FORMAL WRITTEN RESPONSE TO THE LAST OFFICE ACTION IS NOT WAIVED AND MUST INCLUDE THE SUBSTANCE OF THE INTERVIEW (e.g., items 1-7 on the reverse side of this form). If a response to the last Office action has already been filed, then applicant is given one month from this interview date to provide a statement of the substance of the interview.

☐ 2. Since the examiner's interview summary above (including any attachments) reflects a complete response to each of the objections, rejections and requirements that may be present in the last Office action, and since the claims are now allowable, this completed form is considered to fulfill the response requirements of the last Office action. Applicant is not relieved from providing a separate record of the substance of the interview unless box 1 above is also checked.

1-C35

Examiner's Signature

03/19/97
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Attorney Docket No. 46528/102/JOHO 3-20-97

In re patent application of

Jed FAHEY et al.

Serial No. 08/528,858

Filed: September 15, 1995

For: CANCER CHEMOPROTECTIVE FOOD PRODUCTS

Group Art Unit: 1302

Examiner: L. Wong

AMENDMENT AND REQUEST FOR RECONSIDERATION
UNDER 37 C.F.R. § 1.111

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

In response to the Official Action mailed December 24, 1996, applicants respectfully request that the examiner reconsider the propriety of the restriction requirement, as well as the rejection of claims 21-26, 28-34 and 36-38 as obvious over the prior art, in view of the following remarks.

REMARKS

I. INTERVIEW

Applicants and their representative thank Examiner Wong for the courtesies extended during an interview held at the USPTO on March 11, 1997. Examiner Wong indicated that claims 21-26, 28-34 and 36-38 are allowable over the prior art of record.

II. THE RESTRICTION REQUIREMENT

Applicants acknowledge that the examiner made the restriction requirement final in the last Official Action. In a Response to the Restriction Requirement filed October 3, 1996, applicants elected with traverse to prosecute the claims contained in the examiner's Group III (claims 21-26, 28-34 and 36-38). Accordingly, claims 21-26, 28-34 and 36-38 are pending and presented for reconsideration by the examiner, while claims

Serial No. 08/528,858

1-20, 27, 35 and 39-47 are withdrawn from consideration as directed to non-elected inventions.

However, applicants respectfully urge the examiner to reconsider the propriety of the restriction requirement at least with respect to dependent claims 27 and 35. Claim 27 depends from claim 21 and is drawn to a food product rich in glucosinolates made by the process recited in the independent claim. Likewise, claim 35 is also drawn to a food product rich in glucosinolates which, in this instance, is made by the process recited in independent claim 30. It is respectfully asserted that it would not constitute an undue burden for the examiner to consider dependent claims 27 and 35 since the search, and issues of patentability, are similar in scope with respect to all of these claims. Accordingly, it is respectfully urged that the examiner reconsider the propriety of the restriction requirement and examine claims 21-38.

III. THE OBVIOUSNESS REJECTION

Claims 21-26, 28-34, and 36-38 are rejected under 35 U.S.C. §103 as obvious over Patent Abstracts of Japan, Unexamined Applications, Section: C, Sect. No. 305, Vol. 9, No. 2371, p.2. in view of Beecher, Christopher W.W., *Am. J. Clin. Nutr.* 59 (Suppl): 1166-1170S (1994) ("the '94056 application"), Zhang et al., *Proc. Natl. Acad. Sci. USA.* 89: 2399-2403 (1992), Zhang et al., *Cancer Research* 54 (Suppl): 1976-1981S (1994) and Cho et al. U.S. Patent 5,411,986. It is respectfully asserted that the examiner has failed to set forth a *prima facie* case of obviousness.

A. The Prior Art Fails to Teach or Suggest Methods for Preparing Food Products Comprised of the Recited Cruciferous Sprouts or Extracts of These Sprouts

The '94056 application, referred to by the examiner as the "Kenjirou" reference, allegedly provides "a sprout product

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preserved in [a] bag capable of preserving freshness for a long period" (See Abstract.) Beecher summarizes evidence suggesting that consumption of vegetables produced by varieties of *Brassica oleracea*, including broccoli, cauliflower and cabbage, reduce cancer risk. Beecher therefore does not teach or suggest methods for the production of food products comprised of the recited cruciferous sprouts or sprout extracts.

Likewise, the two Zhang articles and the Cho patent fail to teach or suggest methods for the production of food products comprised of the recited cruciferous sprouts or sprout extracts. The Zhang references describe the characterization of anticarcinogenic isothiocyanates found in cruciferous **vegetables**. The Cho patent describes and claims pharmaceutical compositions comprising sulforaphane, and analogues of sulforaphane, that are anticarcinogenic.

The examiner takes the position that:

the process of preparing the product of Kenjiro would be rich in chemoprotective agents as Beecher, Zhang et al (A3), Zhang et al (A10), and Cho et al all teach the cancer preventive properties of *Brassica*.

(paragraph bridging pages 2 and 3). However, the '94056 application fails to teach the claimed methods for preparing food products comprised of the recited cruciferous sprouts or sprout extracts. As will be described in greater detail below, the English language abstract cited by the examiner contains an inaccurate English translation from the Japanese of the invention disclosed in the '94056 application. The '94056 application does not describe a method for preparing broccoli sprouts but provides a method for storing **mature market stage broccoli** to delay yellowing of flower buds.

Serial No. 08/528,858

One embodiment of the invention, claimed in the instant application, is directed to a process comprising the steps of germinating certain cruciferous seeds and harvesting sprouts prior to the 2-leaf stage to form a food product comprising a plurality of these cruciferous **sprouts**. Another embodiment of the claimed invention involves germinating certain cruciferous seeds that produce sprouts having at least 200,000 units per gram fresh weight of Phase 2 enzyme-inducing potential when measured after 3-days of growth and which contain non-toxic levels of indole glucosinolates and their breakdown products and goitrogenic hydroxybutenyl glucosinolates, and harvesting sprouts prior to the 2-leaf stage to form a food product comprising a plurality of **sprouts**. Yet another embodiment of the claimed invention involves extracting glucosinolates and isothiocyanates from the recited cruciferous **sprouts**.

The '94056 application does not describe a method for preparing broccoli **sprouts**. Attached as APPENDIX A is the Translator's Declaration of Mr. Yoichiro Yamaguchi who is familiar with both the Japanese and English languages and is a graduate of Waseda School of Law, Waseda University, Tokyo, Japan and the National Law Center, George Washington University, Washington, D.C. Mr. Yamaguchi is admitted to practice as a patent attorney in Japan and is a registered attorney in the United States. Mr. Yamaguchi translated relevant portions of the '94056 application from the Japanese to the English language and his translation is attached to the Declaration as APPENDIX A1. The '94,056 application is attached as APPENDIX A2.

Following review of the '94056 application and the examiner's first Official Action, Mr. Yamaguchi concludes that:

[t]he English language abstract relied on by the examiner contains an inaccurate description of the '94506 application. Specifically, the '94506 application does not provide a bag capable of preserving the freshness of

Serial No. 08/528,858

broccoli sprouts. Rather, the '94506 application provides a bag capable of preserving the freshness of mature market stage broccoli.

(paragraph 4, emphasis in original.) Accordingly, the '94056 application does not describe a method for preserving broccoli sprouts but describes a method of preserving mature market stage broccoli so that the flower buds do not rapidly yellow and become unmarketable. Accordingly, none of the references, either alone, or in combination, teach or suggest the claimed methods for preparing food products comprised of the recited cruciferous sprouts or extracts made from these sprouts.

B. The Cruciferous Sprouts and Sprout Extracts Prepared According to the Claimed Methods Contain Unexpectedly High Levels of Phase 2 Enzyme Inducer Activity and Unexpectedly Low Levels of Phase 1 Enzyme Inducer Activity

Even assuming the examiner had set forth a *prima facie* case of obviousness, clear evidence of unexpected results contained in the specification has been overlooked. Proof of an unexpected improvement can rebut a *prima facie* case of obviousness. *In re Costello*, 480 F.2d 894, 178 USPQ 290 (CCPA 1973). Specifically, the methods of the instant invention provide food products that have unexpected health benefits compared to food products available in the prior art.

More specifically, the claimed methods of the instant application provide food products comprised of certain cruciferous sprouts, and sprout extracts, with greatly increased levels of Phase 2 inducer activity compared to mature market stage vegetables. As a consequence, a significant health benefit can be realized through ingestion of small quantities of cruciferous sprouts, or sprout extracts, prepared according to the claimed methods. The same health benefits can only be realized, if at all, through the ingestion of impractically large quantities of market stage vegetables that contain significantly

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lower quantities of anticarcinogenic Phase 2 inducer activity compared to the sprouts of the instant invention.

Phase 2 enzymes conjugate functionalized products with endogenous ligands (e.g. glutathione, glucuronic acid, sulfate) and thereby serve primarily a detoxifying role in xenobiotic metabolism. There is very good evidence indicating that when Phase 2 enzymes are induced, animals and cells are protected against the toxic and neoplastic effects of carcinogens. In fact, anticarcinogens have been identified based on their ability to induce Phase 2 enzymes. See, for example, Talalay, Paul, *Chemical Protection Against Cancer by Induction of Electrophile Detoxification (Phase II) Enzymes*, In: CELLULAR AND MOLECULAR TARGETS OF CHEMOPREVENTION, V.E. Steele et al. (eds.), CRC Press, Boca Raton, FL (1992).

The ability of Phase 2 enzyme inducers, such as isothiocyanates, to block carcinogenesis has been known for many years. See, for example, Zhang et al., *Cancer Research* 54 (Suppl): 1976-1981S (1994). In addition, numerous epidemiological studies suggest that high consumption of yellow and green vegetables, especially those of the family Cruciferae and the genus *Brassica* such as cauliflower, cabbage or broccoli, reduces the risk of developing cancer of various organs. See, for example, Graham et al., *J. Natl. Cancer Inst.* 61: 709-714 (1978). However, the quantity of mature market stage vegetables that must be consumed in order to provide even a 50% reduction in cancer risk ratio is so very large as to be difficult for many individuals and further risk reduction is impractical.

Dr. Talalay notes in the accompanying Rule 132 Declaration, attached hereto as APPENDIX B, that consumption of 425 g/wk of mature market stage *Brassica* vegetables, such as broccoli, would result in an odds ratio of approximately 0.5 (50% risk reduction) for colon cancer. It is frequently impractical and many

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individuals cannot tolerate consumption of such a large quantity of market stage broccoli each week. The large quantity of fiber and other phytochemicals associated with consumption of such large quantities of this vegetable is likely to cause bowel irritation and/or flatulence in a significant portion of the population. In addition, many individuals dislike the taste of cruciferous vegetables and will not consume such large quantities for this reason.

Cruciferous sprouts prepared according to the instant invention provide 20 to 50-fold higher levels of Phase 2 enzyme inducer activity than mature, market stage cruciferous vegetables (see APPENDIX B1). Accordingly, much smaller quantities of the sprouts can be consumed to realize the same health benefit obtained through consumption of larger quantities of mature market stage vegetables. Dr. Talalay in the accompanying Rule 132 Declaration calculates that 3 grams of 3-day old sprouts, or 150 milligrams of lyophilized hot water extract of sprouts, contain the same quantity of Phase 2 enzyme inducer activity as 150 grams of mature market stage broccoli. The quantity of mature market stage broccoli, sprouts and sprout extracts that must be consumed to realize the same health benefit (2-1/4 million units of anticarcinogen Phase 2 enzyme inducer activity) is shown in APPENDIX B2 attached to Dr. Talalay's Rule 132 Declaration.

Another unrecognized and unexpected benefit of the claimed methods is to provide food products comprised of certain cruciferous sprouts and sprout extracts that do not contain significant levels of Phase 1 inducer activity, derived from indole glucosinolates. Phase 1 enzymes (cytochromes P-450) functionalize compounds, usually by oxidation or reduction. Although one role of Phase 1 enzymes is to detoxify xenobiotics, several cytochromes P-450 activate various types of procarcinogens to highly reactive ultimate carcinogens.

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Attached to Dr. Talalay's Rule 132 Declaration as APPENDIX B3 are graphs showing comparative paired ion chromatographs of broccoli sprouts and mature market stage broccoli. The paired ion chromatographs were prepared according to the method developed in our laboratory by Prestera *et al.*, *Anal. Biochem.* 239: 168-179 (1996). The principal peaks are glucoraphanin, glucoerucin, glucobrassicin and neoglucobrassicin (APPENDIX B3). The former two glucosinolates are alkylthioglucosinolates with potent Phase 2 enzyme inducer activity and are the predominant glucosinolates found in sprouts. The latter two glucosinolates are indole glucosinolates which predominate in mature market stage broccoli. The indole glucosinolates are (1) very weak Phase 2 enzyme inducers; (2) are bifunctional inducers and therefore induce both Phase 1 and Phase 2 enzymes; (3) degrade to produce condensation products which bind to the Ah receptor and induce certain cytochromes P-450 that activate carcinogens; and (4) may actually enhance carcinogenic activity. Accordingly, the food products of the instant invention not only contain unexpectedly high levels of anticarcinogenic Phase 2 inducer activity but also contain unexpectedly low levels of carcinogenic Phase 1 enzyme inducer activity.

C. Conclusion

The prior art does not teach or suggest methods for production of food products comprised of the recited cruciferous sprouts or sprout extracts. Accordingly, the examiner has failed to set forth a *prima facie* case of obviousness. Although unnecessary to overcome the examiner's obviousness rejection because of the lack of a *prima facie* case of obviousness, evidence of totally unexpected results is presented. The claimed methods of the instant application provide food products comprised of certain cruciferous sprouts, and sprout extracts, with greatly increased levels of Phase 2 inducer activity compared to mature market stage vegetables. In addition, food products prepared according to the claimed invention do not

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contain significant levels of Phase 1 inducer activity which may actually enhance carcinogenic activity. It is therefore respectfully urged that the claims are not obvious over the prior art cited by the examiner and the rejection should be withdrawn.

For all the foregoing reasons, it is respectfully urged that the present claims are in condition for allowance. An early notice to this effect is earnestly solicited. Should there be any questions regarding this application, Examiner Wong is invited to contact the undersigned at the number shown below.

Respectfully submitted,

March 17, 1997
Date

Richard C. Peet
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APPENDIX

A	Translator's Declaration
A1	English language translation of Japanese '94056 application
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A3	Abstract relied upon by examiner
B	Declaration of Paul Talalay Under 37 C.F.R. § 1.132
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B2	Market Stage/3-Day Sprout Stage Broccoli Photograph
B3	Paired Ion Chromatograph (P.I.C.)

A

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Attorney Docket No. 046585/0102

In re patent application of
Jed FAHEY et al.
Serial No. 08/528,858
Filed: September 15, 1995
For: CANCER CHEMOPROTECTIVE FOOD PRODUCTS

TRANSLATOR'S DECLARATION

Commissioner of Patents and Trademarks
Washington, D.C. 20231

Sir:

I, Yoichiro Yamaguchi, being duly warned, hereby declare and say:

1. I am a graduate of Waseda School of Law, Waseda University, Tokyo, Japan and National Law Center, George Washington University, Washington, D.C. I am admitted to practice as a patent attorney in Japan and am a registered attorney in the United States. I am familiar with both the Japanese and English languages.

2. I translated relevant portions of Japanese Laid-Open (Kokai) Patent Application No. 64-94056 ("the '94056 application") from the Japanese to the English language, and this translation is attached hereto as APPENDIX A1. My translation of the '94056 application is a true, faithful and exact translation of the corresponding Japanese language found in the '94056 application. The '94056 application is attached hereto as APPENDIX A2.

3. I have read the examiner's Official Action issued in the above-identified patent application on December 24, 1996 and understand that the examiner has relied on an English language abstract that allegedly describes the contents of the '94056 application. The English language abstract relied on by the

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examiner is attached hereto as APPENDIX A3. (See Patent Abstracts of Japan, Unexamined Applications, Section: C, Sect. No. 305, Vol. 9, No. 2371, p.2.)

4. The English language abstract relied on by the examiner contains an inaccurate description of the '94506 application. Specifically, the '94506 application does not provide a bag capable of preserving the freshness of **broccoli sprouts**. Rather, the '94506 application provides a bag capable of preserving the freshness of mature market stage broccoli. For example, the '94506 application teaches that:

By this invention, broccoli, which easily changes color and produces a bad odor and is conventionally considered to be difficult produce in maintaining freshness, can be preserved for 5 to 7 days in a fresh manner, then commercial value of broccoli can be remarkably increased and the distribution can be expanded.

Examples of the present invention are explained below.

Example 1

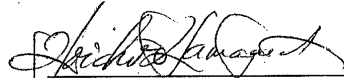
An absorbent with a urethane foam [sheet] having 2mm in thickness and 150mm by 200mm in size, to which 4g of active carbon having 1,700 m²/g specific surface area and having particle size of 90% passing through 100 mesh was added, was enclosed in a bag formed by dual axis extended polypropylene film with a size of 670mm by 550mm, a thickness of 25 μ together with 2 kg of broccoli. The bag was sealed and preserved at a room temperature. Even after 7 days, **yellowing of flower buds** [of broccoli] and bad odor were hardly observed.

(See page 2, lower right column, emphasis added.) Accordingly, the '94056 application does not describe a method for preserving broccoli sprouts but describes a method of preserving mature market stage broccoli so that the **flower buds** do not rapidly yellow and become unmarketable.

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5. The undersigned declares that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent resulting therefrom.

March 17, 1997
Date


Yoichiro Yamaguchi